S/N 09/590,884 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Erika Hawkins et al.	Examiner: M. Chaudhry
Serial No.:	09/590,884	Group Art Unit: 1643
Filed:	June 9, 2000	Docket: 341.014US1
Title:	METHOD FOR INCREASING LUMINESCENCE ASSAY SENSITIVITY	

NOTICE OF APPEAL FROM THE DECISION OF THE EXAMINER TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

BOX AF
Commissioner for Patents
Washington, D.C. 20231

In compliance with 37 C.F.R. § 1.191, Applicants hereby appeal to the Board of Patent Appeals and Interferences from the decision dated November 23, 2001, of the Examiner rejecting claims 1-57 of the above-identified patent application.

A request for oral hearing is submitted herewith along with payment of the required fee.

A request for an extension of time to respond to the Examiner's rejection is submitted herewith along with payment of the required extension fee.

Our check in the amount of $320.00 is enclosed to pay the Notice of Appeal fee under 37 C.F.R. § 1.17(b). Please charge any required additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

ERIKA HAWKINS ET AL.

By Applicants' Attorneys,

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Date 5-23-02 By _____

Robert J. Harris, Ph.D.
Reg. No. 37,346

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to BOX AF, Commissioner of Patents, Washington, D.C. 20231 on **May 23, 2002**.

Anne M. Richards
Name

Anne M Richards
Signature

PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
Erika Hawkins et al.	)	Examiner: Ralph J. Gitomer
Serial No.: 09/590,884	)	Group Art Unit: 1627
Filed: June 9, 2000	)	Docket: 341.014US1
For: METHOD FOR INCREASING LUMINESCENCE ASSAY SENSITIVITY	)	

APPELLANTS' BRIEF ON APPEAL

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Commissioner for Patents
Washington, D.C. 20231

Respectfully submitted,

ERIKA HAWKINS ET AL.

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APPELLANTS' BRIEF ON APPEAL

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APPELLANTS' BRIEF ON APPEAL

Box AF
Commissioner for Patents
Washington, D.C. 20231

Sir:

This Brief is presented in support of the Appeal mailed May 23, 2002 and filed in the U.S. Patent and Trademark Office on June 4, 2002, from the final rejection of claims 1-57 of the above-identified application, as set forth in the Advisory Action mailed July 15, 2002.

This Brief is being submitted in triplicate, as set forth in 37 C.F.R. § 1.192(a). Please charge Deposit Account No. 19-0743 in the amount of $320.00 to cover the fee for filing this Brief. The Commissioner is hereby authorized to charge any additional fee, or credit overpayment, to Deposit Account No. 19-0743.

1. REAL PARTY IN INTEREST

The real party in interest of the above-identified patent application is the assignee, Promega Corporation.

2. RELATED APPEALS AND INTERFERENCES

The Appellants, their legal representatives, and the assignee are not aware of any other appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

3. STATUS OF THE CLAIMS

For the purpose of this appeal, claims 1-57 are pending and stand rejected (see Appendix I).

4. STATUS OF AMENDMENTS

Prior to the Final Office Action, claims 1-75 were pending and were rejected. Claims 76-78 were added by Appellant in response to the Final Office Action. However, claims 58-75 were the subject of a restriction requirement presented in the Final Office Action and claims 76-78 were not entered by the Examiner. Thus, claims 1-57 are pending for the purpose of this appeal.

5. SUMMARY OF THE INVENTION

Reporter molecules are routinely used to monitor molecular events in the field of biology, immunology, cell biology and molecular biology. Reporter molecule that are typically used include radioactive isotopes, flourescent agents, enzymes, and luminescent agents. Luminescent reactions can be used to detect very small quantities of a particular analyte, the substance being identified and measured in an analysis. However, many factors can limit the usefulness of a luminescent assay. For example, luminescence that is not dependent on the presence of an analyte can limit the usefulness of an analytical assay by reducing the ability to accurately measure the quantity of light resulting from the activity of the analyte. As such, there is a need in the art for methods that improve the sensitivity of luminescence assays.

The instant claims are directed to a method for increasing the sensitivity of a bio-luminescent assay comprising carrying out the assay in the presence of an organic compound that reduces luminescence that is not dependent on the presence of an analyte by at least about 10 fold, and that reduces luminescence that is dependent on the presence of an analyte by less than about 7 fold (claim 1), a method for increasing the sensitivity of a luminescent assay comprising carrying out the assay in the presence of an organic compound that reduces luminescence generated by luminogenic molecules not bound to an enzyme by at least about 10 fold, and that reduces the luminescence generated by luminogenic molecules bound to an enzyme by less than about 7 fold (claim 2), a method for increasing the sensitivity of a bio-luminescent assay comprising carrying out the assay in the presence of an organic compound that reduces autoluminescence by at least about 10 fold, and that reduces luminescence that is dependent on the presence of an analyte by less than about 7 fold (claim 3), and a method for increasing the sensitivity of a bio-luminescent assay comprising carrying out the assay in the presence of an organic compound that reduces the luminescence that does not result from a bio-luminescent reaction by at least about 10 fold, and that reduces luminescence that does result from a bio-luminescent reaction by less than about 7 fold (claim35).

Claims 22-24 and 49 are directed to assay kits comprising materials for carrying out the methods of the invention.

6. ISSUES PRESENTED FOR REVIEW

A. Whether the recited term "organic compound" renders claims 1-57 indefinite under 35 U.S.C. § 112, second paragraph.

B. Whether claims 1-3, 8-12, 16-21 and 35-53 are obvious under 35 U.S.C. § 103(a) over the disclosure of JP 0706769A by Mitoma et al.

C. Whether claims 1-3, 8-31 and 34-57 are obvious under 35 U.S.C. § 103(a) over the disclosure of U.S. Patent No. 5,629,168 issued to Kricka.

D. Whether claims 1-57 are obvious under 35 U.S.C. § 103(a) over the disclosure of U.S. Patent No. 5,814,471 issued to Wood.

7. GROUPING OF CLAIMS

For the rejection of claims 1-57 under 35 U.S.C. § 112(2), the claims stand and fall together for the purpose of this appeal.

For the rejection under 35 U.S.C. § 103(a) of claims 1-3, 8-12, 16-21 and 35-53 as being unpatentable over JP 07067696A by Mitoma et al. the claims are grouped as follows:

Group I: Claims 1, 3, 16, 18-19, 21, 35-36, 38-41, 43-45, 47-48 and (8-12 to the extent that they depend from claim 1 or 3); 49-50 and 52-53; and

Group II: Claims 2, 17, 20, 37, 42, 46, and (8-12 to the extent that they depend from claim 2); and 51.

For the rejection under 35 U.S.C. § 103(a) of claims 1-3, 8-31, and 34-57 as being unpatentable over U.S. Patent 5,629,168 issued to Kricka, the claims are grouped as follows:

Group III: Claims 1, 3, 16, 18-19, 21, 35-36, 38-41, 43-45, 47-48 and (8-12 and 14-15 to the extent that they depend from claim 1 or 3); 22, 24, 49-50, 52-54, 56-57, and (25-31 and 34 to extent that they depend from claim 22 or 24); and

Group IV: Claims 2, 17, 20, 37, 42, 46 and (8-12 and 14-15 to the extent that they depend from claim 2); 23, 51, 55 and (25-31 and 34 to the extent that they depend from claim 23).

Group V: Claim 13.

Separate remarks are presented in Section 8 below to address the patentability of the claims in Groups I-V.

For the rejection of claims 1-57 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,814,471 issued to Wood, the claims stand and fall together for the purpose of this appeal.

8. ARGUMENT

I) Rejection Under 35 U.S.C.§ 112, second paragraph.

a) The Applicable Law

In rejecting a claim under the second paragraph of 35 U.S.C.§112, it is incumbent on the

Examiner to establish that one of ordinary skill in the pertinent art, when reading the claims in light of the supporting specification, would not have been able to ascertain with a reasonable degree of precision and particularity the particular area set out and circumscribed by the claims. *Ex parte* Wu, 10 U.S.P.Q. 2d 2031, 2033 (B.P.A.I. 1989)(citing *In re* Moore, 439 F.2d 1232, 169 U.S.P.Q. 236 (C.C.P.A. 1971); *In re* Hammack, 427 F.2d 1378, 166 U.S.P.Q. 204 (C.C.P.A. 1970)). The M.P.E.P. adopts this line of reasoning:

> The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (1) The content of the particular application disclosure;
>
> (2) The teachings of the prior art; and
>
> (3) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. *M.P.E.P.* § 2173.02.

b) Discussion of the Rejection

Claims 1-57 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite due to the recitation of the term "organic compound." Appellants submit that the claim language in question is not indefinite, particularly when analyzed in light of the content of the application disclosure and the claim interpretation that would be given by one of ordinary skill in the art.

The term "organic compound" is defined in the specification at page 10, line 11, as a compound that "comprises one or more carbon atoms." It is submitted that this definition is unambiguous and that it is consistent with the established usage of the term in the art. Therefore, the term "organic compound" is not indefinite.

Additionally, the instant claims recite "an organic compound" that has certain specifically recited properties. For example, in claim 1, the organic compound is present in a bioluminescent assay, and the organic compound "reduces luminescence that is not dependent on the presence of an analyte by at least about 10 fold, and [that] reduces luminescence that is dependent on the presence of an analyte by less than about 7 fold." The specification contains numerous working examples (see pages 18-34) which demonstrate how one skilled in the art can identify an organic compound that possesses the specific properties recited in the claims. Thus, one skilled in the art

can readily identify an "organic compound" and can also readily determine if the organic compound has the recited properties, e.g., reduces luminescence that is not dependent on the presence of an analyte by at least about 10 fold, and reduces luminescence that is dependent on the presence of an analyte by less than about 7 fold as recited in claim 1. Accordingly, the instant claims "particularly point out and distinctly claim the subject matter which the applicant regards as his invention" and are not indefinite. Thus, Appellants urge that claims 1-34 meet the requirements of 35 U.S.C. § 112, second paragraph. Appellants respectfully request that the rejection of claims 1-34 be reversed.

The Examiner's Position

In the Office Action mailed April 24, 2001, the Examiner states that "the term "organic compound" is broad and encompasses more than the specification could possibly support (page 3)" and that "the term "organic compound" is unduly broad especially in view of the examples of suitable organic compounds provided in the specification (page 4)." It is submitted that, even if these statements were correct, they would only be relevant to a rejection under 35 U.S.C. § 112, first paragraph. *In re Swinehart* 169 U.S.P.Q. 226, 229 (C.C.P.A. 1971). However, such a rejection has not been made. Additionally, during a telephonic interview with the Examiner on May 21, 2002, the Examiner confirmed that the rejection had only been made under the second paragraph of 35 U.S.C. § 112. Accordingly, the Examiner's remarks do not support a rejection under 35 U.S.C. § 112, second paragraph.

The Board is also urged to consider that breadth of a claim is not *per se* to be equated with indefiniteness. *In re Gardener*, 166 U.S.P.Q. 138 (C.C.P.A. 1970). A broad claim that merely recites conventional language is not objectionable under 35 U.S.C. § 112(2). Such a claim is neither "too broad in the sense of embracing a concept not stated in the original disclosure nor is it vague or indefinite." *In re Kamel*, 158 U.S.P.Q. 320 (C.C.P.A. 1968).

At page 4 of the Office Action mailed April 24, 2001, the Examiner also states that the term "organic compound" does not adequately define a specific chemical compound or specific class of compounds appropriate for utilization in the recited methods and kits. The claims define such chemical compounds functionally without recitation of a specific chemical structure beyond

the fact that such compounds are organic."

The second paragraph of 35 U.S.C. § 112 does not prohibit the use of a functional description for a claim element. Accordingly, the Examiner has applied an inappropriate legal standard to establish the rejection under 35 U.S.C. § 112, second paragraph. Denial of a patent is not required solely because of the type of language used to define the subject matter for which patent protection is sought. *In re Miller* 169 U.S.P.Q. 597, 599. There is nothing intrinsically wrong in using functional language, defining something by what it does rather than by what it is, in drafting patent claims; courts have even recognized the practical necessity for the use of functional language. *In re Swinehart* 169 U.S.P.Q. 226, 228.

The second paragraph of 35 U.S.C. § 112 only requires that the claims particularly point out and distinctly claim the subject matter which the applicant regards as his invention. As discussed above, one skilled in the art can readily identify an "organic compound," as opposed to an "inorganic compound," and can also readily determine if a given organic compound has the specific properties recited in the claims. Thus, the claims meet the requirements of 35 U.S.C. § 112, second paragraph.

II) Rejections under 35 U.S.C. § 103.

a) The Applicable Law

The Examiner has the burden under 35 U.S.C. § 103 to establish a *prima facie* case of obviousness. *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d (BNA) 1596, 1598 (Fed. Cir. 1988). The M.P.E.P. contains explicit direction to the Examiner that agrees with the court's holding in *In re Fine*:

> In order for the Examiner to establish a *prima facie* case of obviousness, three base criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of

> success must both be found in the prior art, and not based on applicant's disclosure. *M.P.E.P.* § 2142 (citing *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d (BNA) 1438 (Fed. Cir. 1991)).

The Examiner must recognize and consider not only the similarities but also the critical differences between the claimed invention and the prior art. *In re Bond*, 910 F.2d 831, 834, 15 U.S.P.Q.2d (BNA) 1566, 1568 (Fed. Cir. 1990), *reh'g denied*, 1990 U.S. App. LEXIS 19971 (Fed. Cir. 1990).

b) Discussion of the Rejections

Claims 1-3, 8-12, 16-21 and 35-53 are not *prima facie* obvious over Mitoma et al.

Claims 1-3, 8-12, 16-21, and 35-53 were rejected under 35 U.S.C. § 103(a) as being unpatentable over JP 07067696A published by Mitoma et al. However, the Examiner has simply failed to establish a *prima facie* case of obviousness over this brief abstract. Appellants submit that the Examiner has proffered no motivation to modify the enzyme system in *Mitoma* to yield a bioluminescent assay as recited in the instant claims, nor does one exist; that the reference does not provide one skilled in the art with a reasonable expectation that the claimed methods would be operational; and that the claims contain elements not found in the cited art.

Mitoma discusses a method of reducing background luminescence where luminescence is generated by the treatment of a 2,3,-dihydro-1,4-phthalazinedione with heme or peroxidase, in the presence of an oxidizing agent.

Appellants claims are based on their discovery that it is possible to increase the sensitivity of an assay that utilizes a bioluminescent enzyme by selectively reducing unwanted luminescence from non-bioluminescent sources, without similarly reducing the desired signal. This result was unexpected and was not suggested or disclosed in the art.

There are several distinct classes of luminescent reactions. One specific class of luminescent reactions utilizes bioluminescent enzymes, which have unique properties not found in other classes of enzymes associated with luminescent reactions. In particular, bioluminescent enzymes have evolved specifically for the purpose of generating light (see Appellants' specification at page 8, lines 11-17). Appellants believe the structure of bioluminescent enzymes

allows them to minimize luminescence quenching by excluding water (and other quenching molecules) from the excited-state intermediate while light is being produced.

This is not the case with of peroxidase systems, such as the one reported in *Mitoma*. Additionally, bioluminescent enzymes catalyze monooxygenation using molecular oxygen, in contrast to the peroxidase reported in *Mitoma*, which catalyzes single electron transfers using hydrogen peroxide. Accordingly, the mechanism by which bioluminescent reactions generate light differs substantially from the mechanism by which the peroxidase reported in *Mitoma* generates light.

Appellants' Group I claims (claims 1, 3, 16, 18-19, 21, 35-36, 38-41, 43-45, 47-48 and (8-12 to the extent that they depend from claim 1 or 3); 49-50 and 52-53) recite a "bioluminescent assay" or "luminogenic substrate." The Group I claims relate to methods that involve bioluminescent enzyme systems that differ substantially from the peroxidase enzyme reported in *Mitoma*. Appellants' Group II claims (claims 2, 17, 20, 37, 42, 46, and (8-12 to the extent that they depend from claim 2); and 51) recite "luminogenic molecules bound to an enzyme." In the peroxidase system reported in *Mitoma*, there are no "luminogenic molecules bound to enzymes." Thus, the mechanism of the luminogenic reaction in Group II also differs substantially from the mechanism of the peroxidase reaction carried out in *Mitoma*.

The Examiner has not identified any motivation for one skilled in the art to modify the peroxidase system reported in *Mitoma* in the manner necessary to arrive at the instantly claimed methods. Additionally, in light of the considerable differences between the peroxidase system discussed in *Mitoma* and the assay systems recited in the instant claims, it is submitted that *Mitoma* would not have provided one skilled in the art with a reasonable expectation that the instantly claimed methods for improving assay sensitivity could have been successfully carried out. Finally, the claims recite certain assay systems that are not suggested by *Mitoma*. Thus, the claims include elements not suggested by *Mitoma*.

In light of the above remarks, it is respectfully submitted that the Examiner has not met any of the three criteria required to establish a *prima facie* case of obviousness over *Mitoma*. Thus, the Group I and Group II claims are not *prima facie* obvious over *Mitoma*. Appellant respectfully requests the reversal of the rejection of claims 1-3, 8-12, 16-21 and 35-53.

The Examiner's Position

The Examiner stated that "it would have been obvious to one having ordinary skill in the art to have reduced background luminescence from any source using an organic compound as taught by Mitoma et al. since Mitoma et al. teach a general method of reducing background luminescence with specific organic compounds." (Page 5 of the Office Action mailed April 24). It is respectfully submitted that the Examiner's conclusion is incorrect. As discussed above, there are several significant differences between the luminescent system reported in *Mitoma* and the enzyme systems recited in the instant claims, most significantly different mechanisms of producing light. Thus, it would not have been obvious to one having ordinary skill in the art to use the compounds discussed in *Mitoma* to reduce background luminescence in an enzyme system recited in the instant claims. In fact, one skilled in the art would have had no expectation that the compounds discussed in *Mitoma* could be used in a method to selectively reduce background luminescence in a bioluminescent assay as claimed.

Claims 1-3, 8-31, and 34-57 are not *prima facie* obvious over *Kricka*. Claims 1-3, 8-31, and 34-57 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,629,168 issued to *Kricka*. However, the Examiner has failed again to establish a *prima facie* case of obviousness. Appellants submit that no motivation to modify the enzyme system in *Kricka* to yield a bioluminescent assay as recited in the instant claims has been proffered, nor does one exist; that the reference does not provide one skilled in the art with a reasonable expectation that the claimed methods would be operational; and that the claims contain elements not found in the cited art.

Kricka discusses a method for increasing the light output and/or the signal-to-background ratio of light output from a chemiluminescent reaction of dihydrophthalazinedione, a peroxidase enzyme catalyst and an oxidant, by carrying out the reaction in the presence of an enhancer which is an aromatic organo-boron compound.

As discussed above, there are several distinct classes of luminescent reactions. One specific class of luminescent reactions utilizes bioluminescent enzymes, which have unique properties not found in other classes of enzymes associated with luminescent reactions. In

particular, bioluminescent enzymes have evolved specifically for the purpose of generating light (Appellants' specification at page 8, lines 11-17). This is not true of the peroxidases reported in *Kricka*. Additionally, bioluminescent enzymes catalyze monooxygenation using molecular oxygen, in contrast to the peroxidases reported in *Kricka*, which catalyze single electron transfers using hydrogenperoxide. Accordingly, the mechanism by which bioluminescent reactions generate light differs considerably from the mechanism by which the peroxidases reported in *Kricka* generate light.

Appellants' Group III and Group V claims (claims 1, 3, 16, 18-19, 21, 35-36, 38-41, 43-45, 47-48 and (8-15 to the extent that they depend from claim 1 or 3); 22, 24, 49-50, 52-54, 56-57 and (25-31 and 34 to extent that they depend from claim 22 or 24)) recite a "bioluminescent assay" or "luminogenic substrate." Thus, the Group III and Group V claims involve enzyme systems that differ significantly from the peroxidase enzymes reported in *Kricka*. Additionally, Appellants' Group IV and Group V claims (claims 2, 17, 20, 37, 42, 46 and (8-15 to the extent that they depend from claim 2); 23, 51, 55 and (25-31 and 34 to the extent that they depend from claim 23)) recite "luminogenic molecules bound to an enzyme." In the peroxidase system reported in *Kricka* there are no "luminogenic molecules bound to enzymes." The peroxidase enzyme system disclosed in *Kricka* generates light by a significantly different mechanism. Thus, the mechanism of the luminogenic reaction recited in the Group IV claims also differs significantly from the mechanism of the peroxidase reaction carried out in *Kricka*.

The Examiner has not identified any motivation for one skilled in the art to modify the peroxidase systems reported in *Kricka* in the manner necessary to arrive at the instantly claimed methods. Additionally, in light of the considerable differences between the peroxidase system discussed in *Kricka* and the assay system recited in the instant claims, it is submitted that *Kricka* would not have provided one skilled in the art with a reasonable expectation that the instantly claimed methods for improving assay sensitivity could have been successfully carried out. Finally, the claims relate to specific assay systems that are not suggested by *Kricka*. Thus, the claims include elements not suggested by *Kricka*.

In light of the above remarks, it is respectfully submitted that the Examiner has not met any of the three criteria required to establish a *prima facie* case of obviousness over *Kricka*.

Thus, the Group III and Group IV claims are not *prima facie* obvious over *Kricka*. Appellants respectfully request the reversal of the rejection of claims 1-3, 8-31, and 34-57.

Additionally, claim 13 (Group V) recites additional non-obvious features. Appellant's claim 13 recites "the assay is performed in the presence of whole cells." At page 34 of Appellants' specification, it is disclosed that not only can the luminescent assays of the invention be performed on whole cells, but that these assays do not significantly decrease cell viability. Traditionally, such assays have been carried out in solution or in the presence of lysed cell extracts. The ability to carry out the methods of the invention in the presence of whole cells is a useful benefit. For example, it allows for experimental analysis in the same living cells over the course of time. *Kricka* makes no reference to performing assays in the presence of whole cells, and in the examples, *Kricka* only references experiments carried out in solution, not even in the presence of lysed cell extracts. The Examiner has not identified any motivation for one skilled in the art to modify the assay system disclosed in *Kricka* in the manner necessary to arrive at a whole cell system, as recited in claim 13.

Additionally, *Kricka* would not have provided one skilled in the art with any expectation that the organo-boron compounds disclosed therein would provide any useful effect in the presence of whole cells. Finally, *Kricka* does not report any assays using a bioluminescent enzyme or any assay carried out in the presence of whole cells. Therefore, *Kricka* does not disclose or suggest all the elements of claim 13. For this additional reason, claim 13 (Group V) is not *prima facie* obvious over *Kricka*.

The Examiner's Position

At page 6 of the Office Action mailed April 24, 2001, the Examiner stated that "it would have been obvious to one having ordinary skill in the art to have utilized the method taught by Kricka for reducing background luminescence from any source and thus increase luminescent assay sensitivity...." In light of the significant differences between the luminescent system reported in Kricka and the enzyme systems recited in the instant claims, it would not have been obvious to one having ordinary skill in the art to use the methods of Kricka to reduce background luminescence in an enzyme system of the instant claims. In fact, one skilled in the art would

have had no expectation that the compounds discussed in Kricka could be used in a method to selectively reduce background luminescence in a bioluminescent system as claimed.

Claims 1-57 are not *prima facie* obvious over Wood. Claims 1-57 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,814,471 issued to Wood. However, the Examiner has failed to establish a *prima facie* case of obviousness. Appellants submit that no motivation to reduce unwanted luminescence as recited in the instant claims has been proffered; that the reference does not provide one skilled in the art with a reasonable expectation that the claimed methods would be operational; and that the claims contain elements not found in the cited art.

Wood discloses a method for improving the kinetics of light production from luciferase activity (i.e., a rapid increase in light intensity followed by a rapid decrease in the first few seconds, followed by a further decay that may last hours).

The instant claims recite the selective reduction of unwanted luminescence in a bioluminescent assay system. Wood does not suggest that unwanted luminescence can be reduced in any way. Thus, Wood provides no motivation to reduce unwanted luminescence as recited in the instant claims. Additionally, Wood would not have provided one skill in the art with a reasonable belief that unwanted luminescence could be selectively reduced. The instant claims recite selective quenching (for example, see claim 1: "reduces luminescence that is not dependent on the presence of an analyte by at least about 10 fold, and that reduces luminescence that is dependent on the presence of analyte by less than about 7 fold"). Wood provides no suggestion that such selectivity can be achieved. Thus, Wood does not suggest all the elements of the instant claims.

In light of the above remarks, it is respectfully submitted that the Examiner has not met any of the three criteria required to establish a *prima facie* case of obviousness over Wood. Thus, claims 1-57 are not *prima facie* obvious over Wood. Appellants respectfully request the reversal of the rejection of claims 1-57.

The Examiner's Position

At pages 8-9 of the Office Action mailed April 24, 2001, the Examiner states that "Wood et al. is directed to the inclusion of organic compounds in a bioluminescent reaction for the purpose of improving the kinetic[s] of luminescence produced by a luciferin reaction. The claims recite 'a method for increasing the sensitivity of a bioluminescent assay comprising carrying out the assay in the presence of an organic compound...' The method disclosed by Wood et al. would be encompassed by such method."

The Examiner has failed to account for (and omitted from the above passage from the Office Action) an entire portion of the instant claims. The instant claims recite a selective reduction of unwanted luminescence (e.g., "reduces luminescence that is not dependent on the presence of an analyte by at least 10 fold, and that reduces luminescence that is dependent on the presence of an analyte by less than about 7 fold"; claim 1). As stated before, the method reported by Wood solves a completely different problem (improving the kinetics of light production). Wood does not suggest that any reduction of unwanted luminescence can be achieved. Thus, the instantly claimed methods and kits are not *prima facie* obvious over the disclosure of Wood.

At page 9 of the Office Action mailed April 24, 2002, the Examiner states "Since applicant does not provide any structural characteristics of the recited organic compound and merely discloses its functional characteristics, the method taught by Wood et al., of including a thiol containing compound in a luciferase reaction in order to improve luminescence characteristics would obviate the method as claimed." Again, the claims recite a selective reduction of unwanted luminescence. This is an element of the claims. All words in a claim must be considered in evaluating the patentability of that claim against the prior art. *In re Miller* 169 U.S.P.Q. 597, 600. Therefore, the functional language in the instant claims cannot be ignored by the Examiner. Since Wood does not suggest that any reduction of unwanted luminescence can be achieved (a reference must teach or suggest all of the claim limitations to establish a *prima facie* case of obviousness. M.P.E.P. §2142), the instant claims are not *prima facie* obvious over the disclosure of Wood.

9. SUMMARY

It is respectfully submitted that the pending claims are not indefinite. Furthermore, Appellants respectfully submit that the art cited does not render the claimed invention *prima facie* obvious. It is respectfully submitted that claims 1-57 should therefore be allowed. Reversal of the Examiner's rejections of claims 1-57 is respectfully requested.

Respectfully submitted,

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Date 8-23-02 By _____

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to BOX AF, Commissioner of Patents, Washington, D.C. 20231 on August 23, 2002.

Dawn M. Poole
Name

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APPENDIX I

The Claims on Appeal

1. A method for increasing the sensitivity of a bio-luminescent assay comprising carrying out the assay in the presence of an organic compound that reduces luminescence that is not dependent on the presence of an analyte by at least about 10 fold, and that reduces luminescence that is dependent on the presence of an analyte by less than about 7 fold.

2. A method for increasing the sensitivity of a luminescent assay comprising carrying out the assay in the presence of an organic compound that reduces luminescence generated by luminogenic molecules not bound to an enzyme by at least about 10 fold, and that reduces the luminescence generated by luminogenic molecules bound to an enzyme by less than about 7 fold.

3. A method for increasing the sensitivity of a bio-luminescent assay comprising carrying out the assay in the presence of an organic compound that reduces autoluminescence by at least about 10 fold, and that reduces luminescence that is dependent on the presence of an analyte by less than about 7 fold.

4. The method of any one of claims 1-3 wherein the luminescent assay employs a luciferase, aequorin, or obelin enzyme.

5. The method of any one of claims 1-3 wherein the luminescent assay employs firefly luciferase.

6. The method of any one of claims 1-3 wherein the luminescent assay employs *Renilla* luciferase.

7. The method of any one of claims 1-3 wherein the luminescent assay employs *Cypridina* luciferase

8. The method of any one of claims 1-3 wherein the organic compound is present in a concentration of at least 0.1 μM.

9. The method of any one of claims 1-3 wherein the organic compound is present in a concentration of at least 0.1 mM.

10. The method of any one of claims 1-3 wherein the organic compound is present in a concentration of from about 0.1μM to about 500 mM.

11. The method of any one of claims 1-3 wherein the organic compound is present in a concentration of from about 100μM to about 100 mM.

12. The method of any one of claims 1-3 wherein the organic compound is present in a concentration of from about 10 mM to about 100 mM.

13. The method of any one of claims 1-3 wherein the assay is performed in the presence of whole cells.

14. The method of any one of claims 1-3 wherein the assay is carried out in a solvent comprising at least about 10% water by weight.

15. The method of any one of claims 1-3 wherein the assay is carried out in a solvent comprising at least about 25% water by weight.

16. The method of claim 1 wherein the luminescence that is dependent on the presence of an analyte is reduced by less than about 5 fold.

17. The method of claim 2 wherein the luminescence generated by luminogenic molecules

bound to an enzyme is reduced by less than about 5 fold.

18. The method of claim 3 wherein the luminescence that is dependent on the presence of an analyte is reduced by less than about 5 fold.

19. The method of claim 1 wherein the luminescence that is dependent on the presence of an analyte is reduced by less than about 2 fold, remains the same, or is increased.

20. The method of claim 2 wherein the luminescence generated by luminogenic molecules bound to an enzyme is reduced by less than about 2 fold, remains the same, or is increased.

21. The method of claim 3 wherein the luminescence that is dependent on the presence of an analyte is reduced by less than about 2 fold, remains the same, or is increased.

22. An assay kit comprising packaging material containing 1) a luminogenic substrate of a luminescent enzyme, or a luminogenic enzyme; and 2) an organic compound for reducing luminescence that is not dependent on the presence of an analyte by at least about 10 fold, and for reducing luminescence that is dependent on the presence of an analyte by less than about 7 fold.

23. An assay kit comprising packaging material containing 1) a luminogenic substrate of a luminescent enzyme, or a luminogenic enzyme; and 2) an organic compound for reducing luminescence generated by luminogenic molecules not bound to an enzyme by at least about 10 fold, and for reducing luminescence generated by luminogenic molecules bound to an enzyme by less than about 7 fold.

24. An assay kit comprising packaging material containing 1) a luminogenic substrate of a luminescent enzyme, or a luminogenic enzyme; and 2) an organic compound for reducing autoluminescence by at least about 10 fold, and for reducing luminescence that is dependent on the presence of an analyte by less than about 7 fold.

25. The kit of any one of claims 22-24 wherein the enzyme substrate and the compound are each contained in a separate container

26. The kit of any one of claims 22-24 wherein the enzyme substrate and the compound are contained in a single container.

27. The kit of any one of claims 22-24 further comprising a buffer solution suitable for use in a luminescent assay.

28. The kit of claim 27 wherein the enzyme substrate and the buffer solution are contained in a single container.

29. The kit of claim 27 wherein the compound and the buffer solution are contained in a single container.

30. The kit of any one of claims 22-24 further comprising a substrate for a second luminescent enzyme.

31. The kit of any one of claims 22-24 further comprising a quenching agent for a luminescent enzyme reaction.

32. The kit of any one of claims 22-24 wherein the substrate is a substrate for firefly luciferase or *Renilla* luciferase.

33. The kit of any one of claims 22-24 further comprising ATP.

34. The kit of any one of claims 22-24 that comprises both a luminogenic substrate of a luminescent enzyme, and a luminogenic enzyme.

35. A method for increasing the sensitivity of a bio-luminescent assay comprising carrying out the assay in the presence of an organic compound that reduces the luminescence that does not result from a bio-luminescent reaction by at least about 10 fold, and that reduces luminescence that does result from a bio-luminescent reaction by less than about 7 fold.

36. The method of claim 1 wherein the luminescence that is dependent on the presence of an analyte is maintained or increases.

37. The method of claim 2 wherein the luminescence generated by luminogenic molecules bound to an enzyme is maintained or increases.

38. The method of claim 3 wherein the luminescence that is dependent on the presence of an analyte is maintained or increases.

39. The method of claim 35 wherein the luminescence that results from a bio-luminescent reaction is maintained or increases.

40. The method of claim 1 wherein the luminescence that is not dependent on the presence of an analyte is chemi-luminescence that does not result from a bio-luminescent reaction.

41. The method of claim 1 wherein the luminescence that is dependent on the presence of an analyt comprises luminescence generated within a living cell.

42. The method of claim 2 wherein the luminescence generated by luminogenic molecules bound to an enzyme comprises luminescence generated within a living cell.

43. The method of claim 3 wherein the luminescence that is dependent on the presence of an analyte comprises luminescence generated within a living cell.

44. The method of claim 35 wherein the luminescence that does not result from a bio-luminescent reaction comprises luminescence generated within a living cell.

45. The method of claim 1 wherein luminescence that is not dependent on the presence of an analyte comprises luminescence generated by a chemical reaction of coelenterazine or a functional analog thereof.

46. The method of claim 2 wherein the luminescence generated by luminogenic molecules not bound to an enzyme comprises luminescence generated by a chemical reaction of coelenterazine or a functional analog thereof.

47. The method of claim 3 wherein the auto luminescence comprises luminescence generated by a chemical reaction of coelenterazine or a functional analog thereof.

48. The method of claim 35 wherein the luminescence that does not result from a bio-luminescent reaction comprises luminescence generated by a chemical reaction of coelenterazine or a functional analog thereof.

49. An assay kit comprising packaging material containing 1) a luminogenic substrate of an enzyme, or a luminogenic enzyme; and 2) an organic compound for reducing luminescence that does not result from a bio-luminescent reaction by at least about 10 fold, and that reduces luminescence does result from a bio-luminescent reaction by less than about 7 fold.

50. The assay kit of claim 22 wherein the luminescence that is dependent on the presence of an analyte is maintained or increases.

51. The assay kit of claim 23 wherein the luminescence generated by luminogenic molecules bound to an enzyme is maintained or increases.

52. The assay kit of claim 24 wherein the luminescence that is dependent on the presence of an analyte is maintained or increases.

53. The assay kit of claim 49 wherein the luminescence that results from a bio-luminescent reaction is maintained or increases.

54. The assay kit of claim 22 wherein the luminescence that is dependent on the presence of an analyte comprises luminescence generated within a living cell.

55. The assay kit of claim 23 wherein the luminescence generated by luminogenic molecules bound to an enzyme comprises luminescence generated within a living cell.

56. The assay kit of claim 24 wherein the luminescence that is dependent on the presence of an analyte comprises luminescence generated within a living cell.

57. The assay kit of claim 49 wherein the luminescence that does not result from a bio-luminescent reaction comprises luminescence generated within a living cell.

APPENDIX II

Office Actions, Amendments and Responses

Advisory Action mailed 15 July 2002.

Notice of Appeal filed 23 May 2002.

Appellants' Amendment and Response filed 23, May 2002.

Second Office Action Final mailed 23 November 2001.

Appellants' Amendment and Response filed 27 August 2001.

First Office Action mailed 24 April 2001.

APPENDIX III

Relevant Art of Record

Kricka (U.S. Patent No. 5,629,168, issued May 13, 1997).

Mitoma et al. (JP 07067696A, published March 14, 1995).

Wood (U.S. Patent No. 5,814,471, issued September 29, 1998).

APPENDIX IV

Cited Case Law

Ex parte Wu, 10 U.S.P.Q. 2d 2031, 2033 (B.P.A.I. 1989).

In re Bond, 910 F.2d 831, 834, 15 U.S.P.Q. 2d (BNA) 1566, 1568, (Fed Cir. 1990).

In re Fine, 837 F.2d 1071, 1074, 5 U.S.P.Q. 2d (BNA) 1596, 1598 (Fed. Cir. 1988).

In re Gardener, 166 U.S.P.Q. 138 (C.C.P.A. 1970).

In re Hammack, 427 F.2d 1378, 166 U.S.P.Q. 204 (C.C.P.A. 1970).

In re Kamel, 158 U.S.P.Q. 320 (C.C.P.A. 1968).

In re Miller, 169 U.S.P.Q. 597 (C.C.P.A. 1971).

In re Moore, 439 F.2d 1232, 169 U.S.P.Q. 236 (C.C.P.A. 1971).

In re Swinehart, 169 U.S.P.Q. 226 (C.C.P.A. 1971).

In re Vaeck, 947 F.2d 488, 20 U.S.P.Q. 2d (BNA) 1438 (Fed. Cir. 1991).

APPENDIX V

Authorities Relied Upon

35 U.S.C. § 112(2)

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. § 103(a)

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

M.P.E.P. § 2173.02.

The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of:

(1) The content of the particular application disclosure;

(2) The teachings of the prior art; and

(3) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

M.P.E.P. § 2142

In order for the Examiner to establish a *prima facie* case of obviousness, three base criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest

all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.